REMARKS/ARGUMENTS

Claims 1-7 are pending in this application. Claims 1-7 are rejected in the Office action of September 8, 2005. Claim 1 is hereby amended, support for the amendment may be found in original claims 3 and 5. In view of the amendments and remarks made herein, Applicants respectfully request reconsideration of claims 1-7.

Rejections under 35 U.S.C. § 103(a)

Claims 1-7 are rejected under 35 U.S.C. § 103(a) over Cleland *et al.* (US Pat. No. 5,63,605, hereinafter referred to as "Cleland.") Applicants respectfully disagree. Cleland's invention is different from Applicants' invention in several ways. While both Cleland and Applicants disclose the use of PEG and/or poloxamer, the uses are very different from each other. Cleland discloses the use of PEG or poloxamer as an excipient to protect the protein of interest during encapsulation. (See, Cleland, column 9, lines 8-10 and 24-30). Applicants teach the use of PEG and/or poloxamer as pore-forming agents, which effectively make channels in the polymer during biodegradation, thereby allowing acids formed during biodegradation to be washed away from the polymer, thus maintain a microclimate pH of greater than 3 during biodegradation. Stated otherwise, Cleland uses excipients to affect the protein phase during encapsulation, Applicants use pore-forming agents to affect the polymer phase during biodegradation.

Cleland uses PEG or poloxamer to stabilize the antigen of interest during formation of the polymeric delivery system as well as during lyophilization. The problem Cleland solves is stabilize the protein during encapsulation and lyophilization, thus avoiding denaturation of the protein. To achieve this stabilization during encapsulation and lyophilization, Cleland adds excipient to the antigen/protein phase. (See, Cleland, Example 1, specifically column 12, line 50 to column 14, line 35.) The PEG, or poloxamer, stabilizes the antigen of interest during the emulsion phase of the double emulsion method used in Cleland to form the polymeric delivery system as well as during lyophilization. Moreover, the excipients of Cleland are not a pore-forming agents.

The problem Applicants solve in their claimed invention is how to make a polymeric delivery system that is stable during biodegradation. Applicants goal is to stabilize the polymer during biodegradation. Applicants are not using PEG or poloxamer to stabilize their protein during encapsulation. Cleland adds excipient to the protein phase, Applicants add PEG and/or poloxamer to the polymer phase. In direct contrast to Cleland, when Applicants use oil-in-oil emulsion and solvent extraction (O/O) method of encapsulation (see, Specification pages 37-38, carry-over paragraph) no pore-forming agent goes into the antigen phase.

The Office points to Cleland, column 9, lines 24-34 as teaching the use of excipients, including PEG and poloxamer in the amounts of 0.1% to 30% to maintain the stability of the formulation. However, Cleland's use of the excipient is to stabilize the protein of interest during encapsulation. Cleland's excipient is not a pore-forming agent as claimed by Applicants. The 0.1% to 30% (w/v) excipient is based on the aqueous protein phase used in the double emulsion method used in Cleland. Applicants' pore-forming agents, on the other hand, is in the polymer phase, rather than the protein phase. Cleland uses excipients to affect the protein phase, Applicants use excipients to affect the polymer phase.

Moreover, the 0.1% to 30% (w/v) excipient in the protein phase of Cleland is different from the 10% to 30% (w/w), based on polymer, pore-forming agent claimed by Applicant. The Office tries to make the case that one of ordinary skill in the art would know how to use the appropriate amounts of PEG or poloxamer as a pore-forming agent to arrive at a desired pH. However, from the disclosure of Cleland, Applicants do not understand how one of ordinary skill in the art could start with the use of excpient in a buffered encapsulation solution and arrive at the proper amount of pore-forming agent to add to the polymer phase to affect pH during biodegradation. Nowhere does Cleland teach using excipient in the polymer phase. Cleland uses excipient in the protein phase because he's using it to stabilize the protein. There is nothing in Cleland to teach or suggest using an excipient in the polymer phase, where there is no protein to protect. The Office does not explain why one skilled in the art would read Cleland's use of excipient to protect the protein of interest as teaching that the excipient should be added to the phase that contains no protein.

Furthermore, Applicants claimed invention uses a completely different amount of PEG and/or poloxamer than Cleland. Cleland, again, uses 0.1% to 30% (w/v) excipient based on the aqueous protein phase to protect the protein. Applicants use 10% to 30% (w/w), based on polymer, pore-forming agent in the polymer phase. Nowhere in Cleland is the teaching or suggestion to add the specific amount of pore forming agent, 10% to 30% (w/w) claimed by Applicants. Cleland does not teach or suggest use of PEG or poloxamer at a level of 10% to 30% (w/w) based on polymer, which is the range necessary in order for the polymer microclimate to be maintained at a pH above 3 during biodegradation.

With respect to the pH range recited in Cleland, Cleland does teach a pH in the range from 5 to 8 (Cleland, column 9, lines 35-36), as noted by the Examiner. However, this pH is not the microclimate pH experienced during biodegradation. The pH in Cleland is the pH of the buffered, aqueous antigen solution prior to encapsulation. Nothing in Cleland teaches or suggests microclimate pH of greater than 3 during biodegradation. The excipients, added to the buffered, aqueous protein phase, affect the proteins during encapsulation, rather than the polymer during biodegradation. The excipients of Cleland are not added to the polymer phase, they are added to the protein phase; the pH disclosed in Cleland are that of the aqueous protein phase prior to encapsulation not during polymer biodegradation.

Moreover, nowhere does Cleland teach or suggest a method of preparing a biodegradable polymeric delivery system wherein the microclimate pH at greater than 3 during biodegradation. Nowhere does Cleland teach or suggest using from 10% to 30% of a pore-forming agent is necessary in order to achieve this effect. Nowhere does Cleland teach adding 10% to 30% (w/w) of PEG or poloxamer to the polymer in order to achieve this effect. Cleland does not teach or suggest all limitations of the claimed invention.

In conclusion, in light of the amendments and the remarks made herein, Applicants submit that claims 1-7 are now in condition for allowance. Prompt notice of such allowance is respectfully requested.

Respectfully submitted,

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